narcotics and benzodiazepines are often abused and readily available on the street. Alcohol abuse leading to high serum levels causes confusion, but more commonly, it is withdrawal from alcohol that leads to a hyperactive delirium. Alcohol and benzodiazepine withdrawal should be considered in all cases of delirium because even patients who drink only a few servings of alcohol every day can experience relatively severe withdrawal symptoms upon hospitalization.

Metabolic abnormalities such as electrolyte disturbances of sodium, calcium, magnesium, or glucose can cause delirium, and mild derangements can lead to substantial cognitive disturbances in susceptible individuals. Other common metabolic etiologies include liver and renal failure, hypercarbia and hypoxemia, vitamin deficiencies of thiamine and B_{12}, autoimmune disorders including central nervous system (CNS) vasculitis, and endocrinopathies such as thyroid and adrenal disorders.

Systemic infections often cause delirium, especially in the elderly. A common scenario involves the development of an acute cognitive decline in the setting of a urinary tract infection in a patient with baseline dementia. Pneumonia, skin infections such as cellulitis, and frank sepsis also lead to delirium. This so-called septic encephalopathy, often seen in the ICU, is probably due to the release of proinflammatory cytokines and their diffuse cerebral effects. CNS infections such as meningitis, encephalitis, and abscess are less common etiologies of delirium; however, in light of the high mortality rates associated with these conditions when they are not treated quickly, clinicians must always maintain a high index of suspicion.

In some susceptible individuals, exposure to the unfamiliar environment of a hospital itself can lead to delirium. This etiology usually occurs as part of a multifactorial delirium and should be considered a diagnosis of exclusion after all other causes have been thoroughly investigated. Many primary prevention and treatment strategies for delirium involve relatively simple methods to address the aspects of the inpatient setting that are most confusing.

Cerebrovascular etiologies of delirium are usually due to global hypoperfusion in the setting of systemic hypotension from heart failure, septic shock, dehydration, or anemia. Focal strokes in the right parietal lobe and medial dorsal thalamus rarely can lead to a delirious state. A more common scenario involves a new focal stroke or hemorrhage causing confusion in a patient who has decreased cerebral reserve. In these individuals, it is sometimes difficult to distinguish between cognitive dysfunction resulting from the new neurovascular insult itself and delirium due to the infectious, metabolic, and pharmacologic complications that can accompany hospitalization after stroke.

Because a fluctuating course often is seen in delirium, intermittent seizures may be overlooked when one is considering potential etiologies. Both nonconvulsive status epilepticus and recurrent focal or generalized seizures followed by postictal confusion can cause delirium; EEG remains essential for this diagnosis. Seizure activity spreading from an electrical focus in a mass or infarct can explain global cognitive dysfunction caused by relatively small lesions.

It is very common for patients to experience delirium at the end of life in palliative care settings. This condition, sometimes described as *terminal restlessness*, must be identified and treated aggressively because it is an important cause of patient and family discomfort at the end of life. It should be remembered that these patients also may be suffering from more common etiologies of delirium such as systemic infection.

LABORATORY AND DIAGNOSTIC EVALUATION

A cost-effective approach to the diagnostic evaluation of delirium allows the history and physical examination to guide further tests. No established algorithm for workup will fit all delirious patients due to the staggering number of potential etiologies, but one stepwise approach is detailed in Table 34-3. If a clear precipitant is identified, such as an offending medication, further testing may not be required. If, however, no likely etiology is uncovered with initial evaluation, an aggressive search for an underlying cause should be initiated.

Basic screening labs, including a complete blood count, electrolyte panel, and tests of liver and renal function, should be obtained in all patients with delirium. In elderly patients, screening for systemic infection, including chest radiography, urinalysis and culture, and possibly blood cultures, is important. In younger individuals, serum and urine drug and toxicology screening may be appropriate early in the workup. Additional laboratory tests addressing other autoimmune, endocrinologic, metabolic, and infectious etiologies should be reserved for patients in whom the diagnosis remains unclear after initial testing.

Multiple studies have demonstrated that brain imaging in patients with delirium is often unhelpful. If, however, the initial workup is unrevealing, most clinicians quickly move toward imaging of the brain to exclude structural causes. A noncontrast computed tomography (CT) scan can identify large masses and hemorrhages but is otherwise unlikely to help determine an etiology of delirium. The ability of magnetic resonance imaging (MRI) to identify most acute ischemic strokes as well as to provide neuroanatomic detail that gives clues to possible infectious, inflammatory, neurodegenerative, and neoplastic conditions makes it the test of choice. Because MRI techniques are limited by availability, speed of imaging, patient cooperation, and contraindications, many clinicians begin with CT scanning and proceed to MRI if the etiology of delirium remains elusive.

TABLE 34-3 STEPWISE EVALUATION OF A PATIENT WITH DELIRIUM

Initial evaluation
History with special attention to medications (including over-the-counter and herbals)
General physical examination and neurologic examination
Complete blood count
Electrolyte panel including calcium, magnesium, phosphorus
Liver function tests, including albumin
Renal function tests
First-tier further evaluation guided by initial evaluation
Systemic infection screen
Urinalysis and culture
Chest radiograph
Blood cultures
Electrocardiogram
Arterial blood gas
Serum and/or urine toxicology screen (perform earlier in young persons)
Brain imaging with MRI with diffusion and gadolinium (preferred) or CT
Suspected CNS infection: lumbar puncture after brain imaging
Suspected seizure-related etiology: electroencephalogram (EEG) (if high suspicion, should be performed immediately)
Second-tier further evaluation
Vitamin levels: B_{12}, folate, thiamine
Endocrinologic laboratories: thyroid-stimulating hormone (TSH) and free T_4; cortisol
Serum ammonia
Sedimentation rate
Autoimmune serologies: antinuclear antibodies (ANA), complement levels; p-ANCA, c-ANCA. consider paraneoplastic serologies
Infectious serologies: rapid plasmin reagin (RPR); fungal and viral serologies if high suspicion; HIV antibody
Lumbar puncture (if not already performed)
Brain MRI with and without gadolinium (if not already performed)

Abbreviations: c-ANCA, cytoplasmic antineutrophil cytoplasmic antibody; CNS, central nervous system; CT, computed tomography; MRI, magnetic resonance imaging; p-ANCA, perinuclear antineutrophil cytoplasmic antibody.